

REMARKS

Claim 19 has been amended.

Claim 24 has been canceled.

Claim 25 has been amended to correct proper dependency.

Support for the amendment to claim 19 is to be found at paragraph [0029] of the instant application or at page 11, lines 4-5 of the parent international application as published (WO 2005/005657 A1) and at claim 24 as originally filed.

No new matter has been added by these amendments.

Applicants respectfully request entry of the present amendment.

Specification

1) The Examiner has stated that the Application contains sequence disclosures at pages 11, 12, and 19 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a).

Applicants herewith submit an amendment to the specification in the form of a paper copy of a "Sequence Listing" as well as a copy of the "Sequence Listing" in CRF on CD-ROM to comply with the requirements of 37 C.F.R. § 1.821 through 37 C.F.R. § 1.825.

Applicants herewith have amended the specification at pages 11 and 12 to recite SEQ ID NO: 1 (Ala-Ala-Pro-Phe) and SEQ ID NO: 2 (Ile-Glu-Gly-Arg), respectively.

Applicants note that the "Sequence Listing" as submitted is limited to the two tetrapeptide sequences disclosed at pages 11 and 12 and not the tripeptide sequence disclosed at page 19 as referred to by the Examiner in the instant Office action.

Applicants note that 37 C.F.R. § 1.821(a) states, in part:

“Nucleotide and/or amino acid sequences as used in §§ 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. Branched sequences are specifically excluded from this definition. Sequences with *fewer than four* specifically defined nucleotides or amino acids are specifically excluded from this section.” (Emphasis added.)

Applicants therefore respectfully submit that the application disclosed only two unbranched sequences of not fewer than four amino acids. The sequence referred to by the Examiner appearing on page 19 of the disclosure is a derivatized tripeptide (Ala-Ala-Ala) and therefore is specifically excluded from the requirement under 37 CFR § 1.821(a)

2) The Examiner has noted the use of several trademarks in the application that are not in capitalized format. Applicants have amended the disclosure to capitalize all trademarks including those referred to by the Examiner.

Rejections under 35 U.S.C. § 112

3) The Examiner has rejected claims 19-31 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that claim 19 is drawn to a method for detecting protease activity in a sample by contacting the sample solution with a protease substrate and providing conditions under which any protease present in the sample may degrade the protease substrate. The Examiner state that it was unclear how every protease would be detected using any protease substrate.

Applicants have amended claim 1 to recite “A method for detecting protease activity in a sample solution comprising the steps of: (i) contacting the sample solution with a protease

substrate labeled with an electrochemically active marker, wherein the electrochemically active marker is a metallocene moiety, (ii) providing conditions under which a protease present in the sample solution may degrade the protease substrate, wherein the protease is capable of recognizing the protease substrate, and (iii) electrochemically determining information relating to the electrochemically active marker, thereby detecting the protease activity in the sample.” Applicants submit that claim 1 now includes the recitation “wherein the protease is capable of recognizing the protease substrate” thereby clarifying that the protease activity to be detected is a protease in the sample that may degrade the protease substrate.

Applicants further draw the Examiner’s attention to the specification at paragraph [0033] that recites “(p)ptides having more than one cleavage site may be of use, for example, where the substrate is to be used in a screen for general protease activity”.

Applicants respectfully request that the rejection of claim 19 and dependent claims 20-31 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 102(b)

4) The Examiner has rejected claims 19 and 26 under 35 U.S.C. § 102(b) as being anticipated by Hugli (USPN 6,235,494 B1).

The Examiner stated that Hugli teaches a method for detecting manna-binding protein-associated serine protease (MASP) by contacting a sample with a MASP protease electrochemically labeled (linked to) substrate and wherein cleavage of the site recognized by a MASP enzyme results in the electrochemical labels becoming detectable.

Anticipation under 35 U.S.C. 102(b) requires the presence in a single prior art disclosure of each and every element of a claimed invention. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767 (Fed. Cir. 1987), cert. denied, 484 U.S. 1007 (1988).

Applicants have amended claim 1 to recite “A method for detecting protease activity in a sample solution comprising the steps of: (i) contacting the sample solution with a protease substrate labeled with an electrochemically active marker, wherein the electrochemically active marker is a metallocene moiety, (ii) providing conditions under which a protease present in the sample solution may degrade the protease substrate, wherein the protease is capable of recognizing the protease substrate, and (iii) electrochemically determining information relating to the electrochemically active marker, thereby detecting the protease activity in the sample.”

Applicants submit that Hugli does not teach that the electrochemically active marker is a metallocene moiety as recited in claim 19, as amended, and therefore submit that claims 19 and 26 are not anticipated by Hugli..

5) The Examiner has rejected claims 19, 20, 22, and 26 under 35 U.S.C. § 102(b) as being anticipated by Ludin et al. (USPN 6,495,336 B1).

The Examiner stated that Ludin et al. teach a method for detecting protease activity in a sample by contacting a sample solution with a protease substrate labeled (linked to) with an electrochemically active marker under conditions in which protease may cleave off the electrochemically active marker and detecting the electrochemically active marker using the amperometric technique of cyclic voltammetry.

Anticipation under 35 U.S.C. 102(b) requires the presence in a single prior art disclosure of each and every element of a claimed invention. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767 (Fed. Cir. 1987), cert. denied, 484 U.S. 1007 (1988).

Applicants have amended claim 1 to recite “A method for detecting protease activity in a sample solution comprising the steps of: (i) contacting the sample solution with a protease

substrate labeled with an electrochemically active marker, wherein the electrochemically active marker is a metallocene moiety, (ii) providing conditions under which a protease present in the sample solution may degrade the protease substrate, wherein the protease is capable of recognizing the protease substrate, and (iii) electrochemically determining information relating to the electrochemically active marker, thereby detecting the protease activity in the sample.”

Applicants submit that Ludin et al. do not teach that the electrochemically active marker is a metallocene moiety as recited in claim 19, as amended, and therefore submit that claims 19, 20, 22, and 26 are not anticipated by Ludin et al.

6) The Examiner has rejected claims 19, 20, 22, 26, 28, 29, and 30 under 35 U.S.C. § 102(b) as being anticipated by Nagy et al. ((2000) Biosensors & Bioelectronics 15: 265-272).

The Examiner stated that Nagy et al. teach a method for detecting proline iminopeptidase (IP) activity in a sample by contacting the sample with an electrochemically labeled (linked to) IP substrates L-proline *p*-nitroanilide or L-proline β -naphthylamide under conditions suitable for IP to cleave the substrates and detecting the released *p*-nitroanilide or β -naphthylamide using the amperometric technique of cyclic voltammetry.

Anticipation under 35 U.S.C. 102(b) requires the presence in a single prior art disclosure of each and every element of a claimed invention. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767 (Fed. Cir. 1987), cert. denied, 484 U.S. 1007 (1988).

Applicants have amended claim 1 to recite “A method for detecting protease activity in a sample solution comprising the steps of: (i) contacting the sample solution with a protease substrate labeled with an electrochemically active marker, wherein the electrochemically active marker is a metallocene moiety, (ii) providing conditions under which a protease present in the sample solution may degrade the protease substrate, wherein the protease is capable of

recognizing the protease substrate, and (iii) electrochemically determining information relating to the electrochemically active marker, thereby detecting the protease activity in the sample.”

Applicants submit that Nagy et al. do not teach that the electrochemically active marker is a metallocene moiety as recited in claim 19, as amended, and therefore submit that claim 19, and dependent claims 20, 22, 26, 28, 29, and 30, are not anticipated by Nagy et al.

Applicants respectfully request that the rejection of claims 19, 20, 22, 26, 28, 29, and 30 under 35 U.S.C. § 102(b) be withdrawn.

Rejections under 35 USC 103(a)

7) The Examiner has rejected claims 19, 20, 21, 22, 26, 28, and 30 under 35 U.S.C. § 103(a) as being unpatentable over Nagy et al. (2000) in view of Forrest et al. (US Patent No. 4,978,610).

In determining obviousness, “[i]t is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure.” By way of contrast, in determining novelty, a showing that the “prior art reference cited as anticipating a claimed invention. . . lack[ed] the characteristics of the claimed invention. . . would in fact negate the assertion that the claimed invention was described in the prior art.” *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

Although published subject matter is “prior art” for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention. To render a later invention unpatentable for obviousness, the prior art must enable a person of ordinary skill in the field to make and use the later invention *Beckman Instruments*, 892 F.2d at 1551. (*In re Kumar*, Fed. Cir. No. 04-1074).

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.” *Graham v. John Deere Co.*, 148 USPQ 459, 467 (S.Ct. 1966).

As discussed above, Nagy et al. do not anticipate claim 19, as amended. Furthermore, Forrest et al. do not describe or suggest a structure using a protease substrate labeled with a metallocene moiety as an electrochemically active marker and for providing conditions wherein the protease substrate is degraded as recited in claim 1. Combining the teachings of Nagy et al. and Forrest et al. would not have enabled a person of ordinary skill in the field to make and use the instant invention. Therefore, Nagy et al. and Forrest et al. both lack the characteristics of the claimed invention and are different to the claimed invention.

Applicants submit that claim 19, and dependent claims 20, 21, 22, 26, 28, and 30, are therefore not unpatentable over Nagy et al. (2000) in view of Forrest et al. under 35 U.S.C. § 103(a).

Applicants respectfully request that the rejection of claims 19, 20, 21, 22, 26, 28, and 30 under 35 U.S.C. § 103(a) be withdrawn.

8) The Examiner has rejected claims 19, 20, 22, 23, 26, 28, and 30 under 103(a) as being unpatentable over Nagy et al. (2000) in view of Nicholson (US Patent No. 4,456,337).

In determining obviousness, "[i]t is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure." By way of contrast, in determining novelty, a showing that the "prior art reference cited as anticipating a claimed invention. . . lack[ed] the characteristics of the claimed invention. . . would in fact negate the assertion that the claimed invention was described in the prior art." *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

Although published subject matter is "prior art" for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention. To render a later invention unpatentable for obviousness, the prior art must enable a person of ordinary skill in the field to make and use the later invention *Beckman Instruments*, 892 F.2d at 1551. (*In re Kumar*, Fed. Cir. No. 04-1074).

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." *Graham v. John Deere Co.*, 148 USPQ 459, 467 (S.Ct. 1966).

As discussed above, Nagy et al. do not anticipate claim 19, as amended. Furthermore, Nicholson does not describe or suggest a structure using a protease substrate labeled with a metallocene moiety as an electrochemically active marker and for providing conditions wherein the protease substrate is degraded as recited in claim 1. Combining the teachings of Nagy et al. and Nicholson would not have enabled a person of ordinary skill in the field to make and use the instant invention. Therefore, Nagy et al. and Nicholson both lack the characteristics of the claimed invention and are different to the claimed invention.

Applicants submit that claim 19, and dependent claims 20, 22, 23, 26, 28, and 30, are therefore not unpatentable over Nagy et al. (2000) in view of Nicholson under 35 U.S.C. § 103(a).

Applicants respectfully request that the rejection of claims 19, 20, 22, 23, 26, 28, and 30 under 35 U.S.C. § 103(a) be withdrawn.

9) The Examiner has rejected claims 19, 24, 25, 26, 27, and 31 under 103(a) as being unpatentable over Hugli (USPN 6,235,494 B1) in view of Braven et al. (US 2005/0221315 A1).

In determining obviousness, "[i]t is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure." By way of contrast, in determining novelty, a showing that the "prior art reference cited as anticipating a claimed invention. . . lack[ed] the characteristics of the claimed invention. . . would in fact negate the assertion that the claimed invention was described in the prior art." *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

Although published subject matter is “prior art” for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention. To render a later invention unpatentable for obviousness, the prior art must enable a person of ordinary skill in the field to make and use the later invention Beckman Instruments, 892 F.2d at 1551. (In re Kumar, Fed, Cir. No. 04-1074).

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." Graham v. John Deere Co., 148 USPQ 459, 467 (S.Ct. 1966).

As discussed above, Hugli does not anticipate claim 19, as amended. In addition, Applicants respectfully submit that the instant patent application claims priority to GB application number GB 0316075.1, filed 9 July 2003, a date that predates the publication date of Braven et al. by over two years. Applicants note that Braven et al. (US 2005/0221315 A1) has a US publication date of 6 October 2005. Applicants also note that Braven et al. (US 2005/0221315 A1) is a national phase patent application filed under 35 USC § 371 of WO Publication Number WO 2003/074731, published 12 September 2003, a date that is also predated by the claimed priority date of filing of the instant application. Braven et al. is therefore not relevant to the patentability of the instant claims.

Applicants submit that claim 19, and dependent claims 24, 25, 26, 27, and 31, are therefore not unpatentable over Hugli in view of Braven et al. under 35 U.S.C. § 103(a).

Applicants respectfully request that the rejection of claims 19, 24, 25, 26, 27, and 31 under 35 U.S.C. § 103(a) be withdrawn.

10) The Examiner has rejected claims 19, 20, 22, 23, 24, 26, and 27 under 103(a) as being unpatentable over Ludin et al. (USPN 6,495,336 B1) in view of Braven et al. (US 2005/0221315 A1).

In determining obviousness, "[i]t is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure." By way of contrast, in determining novelty, a showing that the "prior art reference cited as anticipating a claimed invention. . . lack[ed] the characteristics of the claimed invention. . . would in fact negate the assertion that the claimed invention was described in the prior art." *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

Although published subject matter is "prior art" for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention. To render a later invention unpatentable for obviousness, the prior art must enable a person of ordinary skill in the field to make and use the later invention *Beckman Instruments*, 892 F.2d at 1551. (*In re Kumar*, Fed. Cir. No. 04-1074).

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." *Graham v. John Deere Co.*, 148 USPQ 459, 467 (S.Ct. 1966).

As discussed above, Ludin et al. do not anticipate claim 19, as amended. As further discussed above, Applicants respectfully submit that claimed priority date of filing of the instant patent application predates the publication dates of Braven et al. and Braven et al. is therefore not relevant to the patentability of the instant claims.

Applicants submit that claim 19, and dependent claims 20, 22, 23, 24, 26, and 27, are therefore not unpatentable over Ludin et al. in view of Braven et al. under 35 U.S.C. § 103(a).

Applicants respectfully request that the rejection of claims 19, 20, 22, 23, 24, 26, and 27 under 35 U.S.C. § 103(a) be withdrawn.


CONCLUSION

With these amendments and arguments, Applicants believe that the application is in condition for allowance. If the US Patent Office believes that communication would further the prosecution of this application, then the appropriate US Patent Office personnel are invited to contact the Applicants' below-signed representative at their earliest convenience.

Please charge Deposit Account No. **50-3194** in the amount of **\$460.00** as set forth in the enclosed transmittal letter. However, if the USPTO determines that an additional fee is due, the Commissioner is hereby authorized to charge Bell & Associates' Deposit Account No. **50-3194**.

Respectfully submitted,

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Matthew R. Kaser, D.Phil.
Reg. No. 44,817

Bell & Associates
201 Warren Drive, Suite 100
San Francisco, California 94131
Phone: (510) 537-2040
Fax: (415) 276-6040